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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/631,845	08/01/2003	Stephen Richmond	078883-0166	1041

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FOLEY AND LARDNER LLP
SUITE 500
3000 K STREET NW
WASHINGTON, DC 20007

EXAMINER	
BOWERS, NATHAN ANDREW	
ART UNIT	**PAPER NUMBER**
1797	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/631,845	RICHMOND ET AL.	
	Examiner	Art Unit	
	NATHAN A. BOWERS	1797	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 July 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22 and 33-42* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-22 and 33-42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *071609*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

1) Claims 1, 2, 5, 6, 10, 18-22, and 36-42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Magnuson (US 20030179916) in view of Hering (US 6146881).

With respect to claims 1, 10, 20-22 and 40-42, Magnuson discloses a method and apparatus for the automated picking of animal cell colonies. This is disclosed in paragraph [0015]. Paragraphs [0068], [0119]-[0130], and [0178] teach that a picking head comprising a hollow pin (Figure 3) is moveable about the apparatus using positioning motors. A dispensing container and a sample container including a plurality of animal cell colonies held in a medium are placed onto the apparatus according to paragraphs [0117] and [0132]. Magnuson discloses in paragraphs [0015] and [0059] that the dispensing container comprises an array of wells separated by a characteristic spacing. Paragraph [0068] states that machine vision and image processing features are used to identify animal cell colony locations in the sample container, and the picking head is moved to above the sample container in response. Specifically, paragraphs [0018] and [0074] disclose a camera as a useful image capturing device, and paragraphs [0099]-[0102] disclose image processing software. Paragraph [0069] and [0117] teach that the hollow pin is aligned with the animal cell colony locations, and that a distal end of the hollow pin is introduced into the cell medium proximate to the animal cell colony by an offset distance. Cells are aspirated into the hollow pin and expelled into the dispensing container through the movement of the picking head. Magnuson, however, does not expressly state that the animal cell colonies have a size smaller than

the inside diameter of the hollow pin. Magnuson additionally does not expressly state that the hollow pin comprises an inner pin and an outer pin.

Hering discloses a method for collecting cells from a liquid bath comprising the use of a picking head. The picking head includes a hollow pin that is subdivided into two parts: an inner hollow pin (Figure 5B:c) and an outer hollow pin (Figure 5B:a). This is disclosed in column 8, line 66 to column 9, line 15. Hering teaches that the outer pin and inner pin can be fixedly or detachably attached to one another, and that the inner and outer pins are each moved together between various collection locations by a liquid conveying device (Figure 6:64). It can be inferred that collected cells and/or cell groups are smaller in diameter than the outer hollow pin because the outer hollow pin serves as a perfusion ring that traps all fluid and particles within the ring during aspiration.

Magnuson and Hering are analogous art because they are from the same field of endeavor regarding the collection and transportation of cells using a suction device.

At the time of the invention, it would have been obvious to provide an outer hollow pin surrounding the inner hollow pin disclosed by Magnuson so that the outer hollow pin is larger than the diameter of the individual collected cell colonies. Hering teaches that the use of an additional outer hollow pin of a large diameter is beneficial because it can be used to isolate a particular cell collection area during aspiration. Hering states that the outer hollow pin would serve to define a discrete treatment area within a liquid bath, thus preventing contamination during collection.

With respect to claim 2, Magnuson and Hering disclose the method in claim 1. Magnuson additionally teaches that the picking step comprises repeating the aligning and aspirating steps for the hollow pin in order to pick multiple ones of the animal cell colonies. This is taught in paragraph [0059].

With respect to claims 5 and 6, Magnuson and Hering disclose the method in claim 1. In addition, Magnuson teaches that the animal cell colonies are stained either with a contrast enhancing agent or a fluorescent agent to assist the imaging processing. In paragraph [0111], Magnuson teaches that dark field microscopy and fluorescence-assisted detection can be employed in the invention.

With respect to claims 18 and 19, Magnuson and Hering disclose the method in claim 1. In addition, Magnuson teaches that the animal cell colony comprises either a plurality of cells or a single cell. Paragraphs [0116]-[0118] teach that the invention may be used to process a plurality of cells or a single cell.

With respect to claims 36-39, Magnuson and Hering disclose the method and apparatus in claims 1 and 10. Magnuson, further teaches that the offset distance between the distal end of the pin and the base of the container is dictated by the vertical height of the adherent animal cell colony. Accordingly, if colonies with heights of 0.25 to 1.0 mm are present, then the offset distance between the pin and the base during collection will be 0.25 to 1.0 mm.

2) Claims 3, 13 and 33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Magnuson (US 20030179916) and Hering (US 6146881) as applied to claims 1 and 10, and further in view of Bienert (US 20010019845).

Magnuson and Hering disclose the method and apparatus set forth in claims 1 and 10 as set forth in the 35 U.S.C. 103 rejection above, however, do not expressly disclose a plurality of hollow pins are used in the collection of animal cells.

Bienert discloses a picking head comprising a plurality of pins capable of automatically transporting biological cells from a sample container to a dispensing container. This is taught in paragraphs [0035]-[0045] and generally throughout the reference. Pins are selectively moved into a transfer position and simultaneously or independently activated in order to collect samples in parallel. It is apparent from Figure 2 that Bienert's invention is capable of aligning with the characteristic spacing of a well plate array.

Magnuson and Bienert are analogous art because they are from the same field of endeavor regarding the automatic collection and dispersion of biological samples.

At the time of the invention, it would have been obvious to ensure that the invention disclosed by Magnuson contained a plurality of hollow pins each individually aligned with the characteristic spacing of the wells located in the dispensing container. The simultaneous processing of a plurality of samples in parallel is advantageous because the sampling process can be accomplished more quickly with better accuracy. The use of multiple hollow tubes correlating to multiple wells reduces cross

contamination since different tubes are used to collect different samples. The process can be easily automated to enhance reproducibility.

3) Claims 4, 11, 12, 34 and 35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Magnuson (US 20030179916) and Hering (US 6146881) as applied to claims 1 and 10, and further in view of Sogi (US 4210724).

Magnuson and Hering disclose the apparatus and method set forth in claims 1 and 10 as set forth in the 35 U.S.C. 103 rejection above. In addition, Magnuson discloses in paragraphs [0011] and [0020] that the animal cell colonies are adhered to the sample container and immersed in a medium. Magnuson, however, does not expressly disclose that the distal end of the pin is agitated relative to the sample container so as to produce turbulence in the medium to detach the animal cell colony at the location prior to performing the aspirating step. Magnuson does not disclose a drive mechanism for causing lateral or rotary motion of the distal ends of the pins to facilitate detachment of animal cell colonies.

Sogi discloses an apparatus for automatically transporting cells in a culturing solution to a dispensing container by collecting the desired cells in a pipette through suction. This is taught in the abstract and in column 10, line 54 to column 11, line 48. Column 11, line 49 to column 13, line 16 teach that a drive mechanism is provided to cause the tip of the pipette to quickly oscillate in the culture solution during collection in order to facilitate detachment of cell colonies adhered to the sample container. The pipette is fully capable of performing both lateral and rotary oscillations.

Magnuson and Sogi are analogous art because they are from the same field of endeavor regarding the automatic collection and transportation of cultured cells.

At the time of the invention, it would have been obvious to provide Magnuson's invention with a drive mechanism capable of oscillating the distal ends of the pins in order to facilitate, during collection, the detachment of animal cell colonies adhered to the sample container. Sogi teaches in column 3, lines 36-40 and column 13, lines 33-42 that automatic agitation of the culture solution is a highly efficient way to ensure that the cells are suspended in the sample and fully gather during the collection process. Magnuson teaches in paragraph [0011] that animal cells are characterized by a high affinity for the surfaces upon which they are immobilized during growth. In this way, agitation and scraping forces would have been necessary to dislodge the adherent cells from their growth substrates. Therefore, it would have been obvious to use the distal ends of the tips to dislodge the target cells by producing turbulence in the medium.

4) Claims 4, 7-9, 11, 12 and 14-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Magnuson (US 20030179916) and Hering (US 6146881) as applied to claims 1 and 10, and further in view of Parekh (US 6064754).

With respect to claims 4, 11 and 12, Magnuson and Hering disclose the method set forth in claim 1 as set forth in the 35 U.S.C. 103 rejection above. In addition, Magnuson discloses in paragraphs [0011] and [0020] that the animal cell colonies are adhered to the sample container and immersed in a medium. Magnuson, however, does not expressly disclose that the distal end of the pin is agitated relative to the

sample container so as to produce turbulence in the medium to detach the animal cell colony at the location prior to performing the aspirating step.

Parekh discloses a computer assisted isolation system for removing biological material from selected spots on a biological plate. Column 7, lines 13-20 state that proteins are fluorescently labeled and detected by an image processing means, and column 13, lines 15-55 indicate that an automated picking apparatus is provided for collecting a desired protein through suction and moving the sample to a separate dispensing container for analysis. Column 13, line 56 to column 14, line 7 teaches that the tips of the picking apparatus are agitated relative to the sample container in order to collect the target material. This agitation intrinsically must produce turbulence in the medium.

Magnuson and Parekh are analogous art because they are from the same field of endeavor regarding the automatic imaging, collection, and dispensing of biological components.

At the time of the invention, it would have been obvious to agitate the distal ends of the pins located in the picking apparatus disclosed by Magnuson. Magnuson teaches in paragraph [0011] that animal cells are characterized by a high affinity for the surfaces upon which they are immobilized during growth. In this way, agitation and scraping forces would have been necessary to dislodge the adherent cells from their growth substrates. Therefore, it would have been obvious to use the distal ends of the tips to dislodge the target cells through direct contact or by producing turbulence in the medium.

With respect to claims 7-9 and 14-16, Magnuson and Hering disclose the method and apparatus set forth in claims 1 and 10 as set forth in the 35 U.S.C. 103 rejection above, however do not expressly disclose that the plurality of animal cell colonies comprise or express a biological molecule of interest, namely biopharmaceutical proteins.

Parekh discloses a computer assisted isolation system for removing biological material from selected spots on a biological plate. Column 2, lines 8-20 and column 4, lines 20-51 teach that the biological material may comprise biopharmaceutical proteins expressed from a cell culture. Column 7, lines 13-20 state that the proteins are fluorescently labeled and detected by an image processing means, and column 13, lines 15-55 indicate that an automated picking apparatus is provided for collecting a desired protein through suction and moving the sample to a separate dispensing container for analysis.

At the time of the invention, it would have been obvious to use Magnuson's invention to selectively aspirate and dispense animal cells that express biological molecules, and, more specifically, biopharmaceutical proteins. In column 2, lines 8-20, Parekh teaches that the presence, absence, or altered expression of many different proteins can be associated with a disease or a condition of interest. Studying the expression of these products using Magnuson's device would therefore been advantageous in order to better understand physiological problems associated with difficulties in gene expression. Furthermore, biomolecules are often useful as

therapeutic agents, and as markers for diagnosis, prognosis, and evaluating response to treatment. Therefore, it would have been beneficial to develop methods designed to detect, isolate, and consolidate animal cells that express biopharmaceutical proteins in order to produce a cell product that has valuable medicinal or therapeutic applications.

With respect to claim 17, Magnuson and Hering disclose the method set forth in claim 1 as set forth in the 35 U.S.C. 103 rejection above, however do not expressly disclose that the animal cell colonies are held suspended in the medium.

Parekh discloses a computer assisted isolation system for removing biological material from selected spots on a biological plate. Column 7, lines 13-20 state that proteins are fluorescently labeled and detected by an image processing means, and column 13, lines 15-55 indicate that an automated picking apparatus is provided for collecting a desired protein through suction and moving the sample to a separate dispensing container for analysis. Column 2, lines 21-49 teach that the target biological materials are suspended in a semi-solid gel prior to collection by the picking apparatus.

At the time of the invention, it would have been obvious to suspend the animal cells disclosed by Magnuson in a semi-solid gel rather than allowing the cells to adhere to the sample container. In column 6, lines 2-12, Parekh teaches that gels are capable of suspending biological materials prior to collection, and are non-interfering with respect to fluorescence detection and image processing. Applicant teaches on page 1 of the specification that mammalian cell colonies held in suspension in a semi-solid medium are well known in the art.

Response to Arguments

Applicant's arguments filed 16 July 2009 with respect to the 35 U.S.C. 103 rejections involving Magnuson and Hering have been fully considered but they are not persuasive.

Applicant's principle arguments are

(a) There would be no motivation to add the Hering perfusion ring to the hollow pin of Magnuson because Magnuson already teaches that an isolating seal is provided. Any additional perfusion ring would therefore be wholly redundant and would serve no purpose.

In response please consider the following remarks.

It is agreed that Magnuson expresses an intent in paragraph [0172] to form a tight seal over a portion of the colony to be aspirated. In spite of this expressed desire, one of ordinary skill in the art would have recognized that a tight seal may not always be realized due to a variety of practical problems, such as variations in the contours of the colony and/or pin tip. Furthermore, one of ordinary skill would have recognized that contamination would be an issue if suction is implemented moments before or after a full seal is produced between the cell colony and the tip of the inner pin. Accordingly, it would have been obvious to utilize the Hering perfusion ring when practicing the method/apparatus of Magnuson as a "back up" to ensure that contamination is prevented even if the seal between inner pin tip and cell colony is unintentionally broken at any time.

(b) Any perfusion ring added to Magnuson cannot be read onto the hollow pin of claim 1 because fluid is not aspirated into the Hering perfusion ring.

In response please consider the following remarks.

Hering indicates in Figure 5b and column 9, lines 10-15 that the outer pin (i.e. perfusion ring) of Hering covers the entire cylindrical surface of the inner pin (c). Since cells are aspirated through the inner pin, they are also aspirated through the outer pin because the outer pin envelopes the entire body of the inner pin. This is entirely consistent with the operation of Applicant's claimed invention described in Figure 7 and pages 12-13 of the instant specification. If Applicant is arguing that the claims require cells to be sucked through the annular region between the inner and outer pins, then the claims are not enabled by the specification.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nathan A. Bowers whose telephone number is (571) 272-8613. The examiner can normally be reached on Monday-Friday 8 AM to 5 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Marcheschi can be reached on (571) 272-1374. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/William H. Beisner/
Primary Examiner, Art Unit 1797

/Nathan A Bowers/
Examiner, Art Unit 1797